What is claimed is:

1. A method of diagnosing cleft lip and/or palate or other disease states associated with IRF6 dysfunction or dysregulation in a subject, comprising:
obtaining a biological sample from said subject; and
detecting a polymorphism in a IRF6 nucleic acid, wherein the presence of a polymorphism associated with cleft lip and/or palate or other disease state associated with an IRF6 dysfunction or dysregulation.

2. The method of claim 1, wherein said polymorphism is in exons 2-9 of said IRF6 encoding nucleic acid.

3. The method of claim 1, wherein said nucleic acid is a sequence which encodes a polypeptide sequence comprising amino acids 13-113 of SEQ ID NO:2, wherein said polypeptide comprises at least one polymorphism associated with an IRF6 dysfunction or dysregulation.

4. The method of claim 1, wherein said nucleic acid is a sequence which encodes a polypeptide sequence comprising amino acids 226-394 of SEQ ID NO:2, wherein said polypeptide comprises at least one polymorphism associated with an IRF6 dysfunction or dysregulation.

5. The method of claim 3, wherein said polymorphism is a change from an arginine to cysteine at amino acid residue 84 (Arg84Cys).

6. The method of claim 3, wherein said polymorphism is a change from an arginine to histidine at amino acid residue 84 (Arg84His).

7. The method of claim 5, wherein said polymorphism is characterized by a loss of contact with a DNA binding domain of IRF6.

8. The method of claim 6, wherein said polymorphism is characterized by a loss of contact with a DNA binding domain of IRF6.

9. A method of diagnosing an IRF6 dysfunction or dysregulation in a subject, said method comprising:

obtaining a biological sample from said subject;

detecting the presence of at least one polymorphism as set forth in Table 1 in IRF6 in said sample, wherein the presence of said polymorphism is indicative of said subject having an IRF6 dysfunction or dysregulation.

10. A method of diagnosing a susceptibility or propensity to Van der Woude syndrome, Poplitieal pterygium syndrome, or isolated cleft lip and/or palate in a subject, comprising:

obtaining a biological sample from said subject; and

detecting a polymorphism in an IRF6 encoding nucleic acid present in said sample, wherein the presence of said polymorphism in is indicative of said subject being susceptible to or having a propensity for Van der Woude syndrome, Poplitieal pterygium syndrome, or isolated cleft lip and/or palate.

11. A method of diagnosing a susceptibility to Van der Woude syndrome, Poplitieal pterygium syndrome, or isolated cleft lip and/or palate, comprising

obtaining a biological sample from said subject; and

detecting an alteration in the activity of a polypeptide encoded by an IRF6 gene in a test sample, in comparison with the activity of a polypeptide encoded by IRF6 gene in a control sample, wherein the presence of an alteration in activity of the polypeptide in the test sample is indicative of a susceptibility to Van der Woude syndrome, Poplitieal pterygium syndrome, or isolated cleft lip and/or palate.

12. A method for screening a subject predisposed or susceptible an IRF6-related disorder associated with a genetic polymorphism in the IRF6 gene, said method comprising:

providing a biological sample from the subject; and

testing the sample for the presence of one or more nucleotide mutations from nucleotide

positions 1-2171 of SEQ ID NO: 1, wherein, the presence of the mutation indicates that the subject is genetically predisposed to an IRF6-related disorder.

13. A method of diagnosing susceptibility to isolated cleft lip and/or palate in a subject, comprising:

obtaining a biological sample from said subject; and

detecting a polymorphism in a IRF6 gene product, wherein the presence of an amino acid change from a valine to an isoleucine at amino acid residue 274 (Val274Ile) in said gene product is indicative of said subject having a susceptibility to isolated cleft lip and/or palate.

14. A method for diagnosing susceptibility to isolated cleft lip and/or palate in an individual, comprising:

screening for an at-risk genotype in a IRF6 nucleic acid that is more frequently present in an individual susceptible to isolated cleft lip and/or palate (affected), compared to the frequency of its presence in a healthy individual (control), wherein the presence of the at-risk genotype is indicative of a susceptibility to isolated cleft lip and/or palate.

15. The method of claim 14, wherein said at-risk genotype is characterized as a VV genotype at allele 274 of an IRF6 gene product.

16. A method for diagnosing an individual at-risk for isolated cleft lip and/or palate associated with a V allele in an IRF6 gene product comprising:

providing a biological sample from said individual;

determining the genotype of said individual at nucleic acid corresponding to a V274I site of an IRF6 gene product, wherein an individual with two valine encoding alleles at the nucleic acid corresponding to said V274I site possess an at-risk genotype associated with isolated cleft lip and/or palate.

17. The method of claim 16, wherein a valine/valine (VV) encoding genotype is at an increased risk of isolated cleft lip and/or palate than an individual with an isoleucine/isoleucine (I/I) encoding genotype.

18. The method of claim 16, wherein a valine/valine (VV) encoding genotype is at an increased risk of isolated cleft lip and/or palate than an individual with a valine/isoleucine (VI) encoding genotype.

19. A method for screening a subject predisposed or susceptible to Van der Woude syndrome, Poplitieal pterygium syndrome, or isolated cleft lip and/or palate associated with a genetic polymorphism in the IRF6 gene, said method comprising:
providing a biological sample from the subject; and
testing the sample for the presence of one or more nucleotide mutations from nucleotide positions 1-2171 of SEQ ID NO: 1, wherein, the presence of the mutation as shown in Table 1 indicates that the subject is genetically predisposed to Van der Woude syndrome, Poplitieal pterygium syndrome, or isolated cleft lip and/or palate.

20. A method of determining a risk for an IRF6 dysfunction or dysregulation or propensity thereto in a subject, said method comprising:
obtaining a biological sample from said subject;
analyzing the IRF6 nucleic acid in said sample; and
determining the presence of at least one mutation as set forth in Table 1 of IRF6, wherein the presence of said mutation is indicative of a risk for an IRF6 dysfunction or dysregulation or propensity thereto in said subject.

21. The method of claim 20, wherein said IRF6 dysfunction or dysregulation is selected from the group consisting of: Van der Woude syndrome, Poplitieal pterygium syndrome, and isolated cleft lip and/or palate.

22. A method of identifying a polymorphism associated with an IRF6 dysfunction or dysregulation comprising:

isolating a nucleic acid of SEQ ID NO:1 from a plurality of subgroup of subjects, wherein one subgroup has no prevalence for a IRF6 associated disease and at least one or more subgroups which do have a prevalence for a IRF6 associated disease; and

identifying a polymorphism as set forth in Table 1 by comparing the nucleotide sequence of the nucleic acid of the one subgroup having no prevalence for an IRF6 associated disease with the at least one or more subgroups having a prevalence for an IRF6 associated disease.

23. A method of detecting a polymorphism associated with an IRF6 dysfunction or dysregulation comprising:

obtaining a biological sample from said subject; and

detecting a nucleic acid molecule comprising an IRF6 nucleic acid having the nucleotide sequence of SEQ ID NO:1 and comprising at least one polymorphism as shown in Table 1.

24. The method of claim 23, wherein said IRF6 dysfunction or dysregulation is selected from the group consisting of: Van der Woude syndrome, Poplitieal pterygium syndrome, and isolated cleft lip and/or palate.

25. A method of identifying an agent which modulates activity of a polypeptide encoded by an IRF6 nucleic acid, wherein said polypeptide comprises an amino acid sequence as depicted in SEQ ID NO:2 and comprises at least one polymorphism as shown in Table 1 comprising:

contacting said polypeptide variant with an agent to be tested;

assessing the level of activity of the IRF6 variant polypeptide; and

comparing the level of activity with a level of activity of said variant polypeptide in the absence of the agent, wherein if the level of activity of the polypeptide in the presence of the agent differs, by an amount that is statistically significant from the level in the absence of the agent, then the agent is an agent that modulates activity of a variant IRF6 polypeptide.

26. A method of identifying an agent which alters expression of a variant IRF6 nucleic acid, comprising:

contacting a variant nucleic acid comprising SEQ ID NO:1 and comprising at least one polymorphism at shown in Table 1 with an agent to be tested;

assessing the level of expression of said variant nucleic acid; and

comparing the level of expression with a level of expression of said variant nucleic acid in the absence of the agent, wherein if the level of expression of the nucleotide in the presence of the agent differs, by an amount that is statistically significant, from the expression in the absence of the agent, then the agent is an agent that alters expression of a variant IRF6 nucleic acid.

27. A method of identifying and obtaining an inhibitor of the activity of a polypeptide, or a derivative, or fragment thereof comprising the amino acid sequence of SEQ ID NO:2 which comprises at least one polymorphism as shown in Table 1, comprising:

contacting said polypeptide, or derivative, or fragment thereof with a test agent for inhibiting activity, in the presence of compounds that provide a detectable symbol in response to test agent activity; and

detecting the presence or absence of a signal or increase or decrease of a signal generated from inhibiting activity, wherein the absence or decrease of the signal is indicative inhibiting activity of said polypeptide.

28. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of said IRF6 nucleic acid to said immobilized targets on said solid support.

29. The method of claim 28, wherein a binding of a variant IRF6 nucleic acid to said immobilized targets on said solid support is indicative of the presence, absence, or prevalence of an IRF6 dysfunction or dysregulation.

30. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of an IRF6 nucleic acid

comprising the nucleotide sequence of SEQ ID NO:1 and comprising at least one polymorphism as shown in Table 1.

31. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of a vector, wherein said vector comprises an isolated nucleic acid comprising SEQ ID NO:1 and comprising at least one polymorphism as shown in Table 1, operatively linked to a regulatory sequence to said immobilized targets on said solid support.

32. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of a recombinant host cell, present in said sample.

33. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of an isolated polypeptide encoded by an IRF6 nucleic acid present in said sample, said polypeptide comprising:

(a) the amino acid sequence as depicted in SEQ ID NO:2 which comprises at least one polymorphism as shown in Table 1;

(b) the amino acid sequence as depicted in SEQ ID NO:2 which comprises at least two polymorphisms as shown in Table 1;

(c) an amino acid sequence which is greater than about 90% identical to an amino sequence of SEQ ID NO:2 and comprising at least one polymorphism as shown in Table 1; and

(d) an amino acid sequence which is greater than about 95% identical to an amino acid sequence of SEQ ID NO:2 and comprising at least one polymorphism as shown in Table 1.

34. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of an antibody, or a fragment thereof, that specifically binds to the polypeptide encoded by an IRF6 nucleic acid comprising:

(a) the amino acid sequence as depicted in SEQ ID NO:2 which comprises at least one polymorphism as shown in Table 1;

(b) the amino acid sequence as depicted in SEQ ID NO:2 which comprises at least two polymorphisms as shown in Table 1;

(c) an amino acid sequence which is greater than about 90% identical to an amino sequence of SEQ ID NO:2 and comprising at least one polymorphism as shown in Table 1; and

(d) an amino acid sequence which is greater than about 95% identical to an amino acid sequence of SEQ ID NO:2 and comprising at least one polymorphism as shown in Table 1.

35. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of a nucleic acid molecule comprising exons 2-9 of IRF6 having a nucleotide sequence comprising SEQ ID NO:1 and comprising at least one polymorphism associated with Van der Woude syndrome, Poplitieal syndrome, and isolated cleft lip and/or palate in any one of said exons.

36. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of an IRF6 nucleic acid having a nucleotide sequence depicted in SEQ ID NO:1, wherein said nucleotide sequence encodes a polypeptide sequence comprising amino acids 13-113 of SEQ ID NO:2, wherein said polypeptide comprises at least one polymorphism as shown in Table 1.

37. The method of claim 1, wherein said detecting comprising contacting said sample with a solid support under conditions allowing interaction of an IRF6 nucleic acid having a nucleotide sequence depicted in SEQ ID NO:1, wherein said nucleotide sequence encodes a polypeptide sequence comprising amino acids 226-394 of SEQ ID NO:2, wherein said polypeptide comprises at least one polymorphism as shown in Table 1.

38. A diagnostic composition for detecting the predisposition to an IRF6 dysfunction or dysregulation, the composition comprising at a nucleic acid comprising SEQ ID NO:1 and comprising at least one polymorphism, and a carrier.

39. The diagnostic composition of claim 38 comprising a nucleic acid sequence comprising SEQ ID NO:1 and comprising at least one polymorphism as shown in Table 1, and a carrier.

40. A transgenic non-human animal comprising

(a) a nucleic acid molecule comprising an IRF6 nucleic acid having the nucleotide sequence having SEQ ID NO:1 and comprising at least one polymorphism as shown in Table 1;

(b) a nucleic acid molecule comprising an IRF6 gene, the nucleotide sequence of SEQ ID NO:1 encoding a polypeptide comprising an amino acid sequence as depicted in SEQ ID NO:2 and comprises at least one polymorphism associated as shown in Table 1.

41. An isolated nucleic acid molecule comprising:

(a) a nucleic acid molecule comprising an IRF6 nucleic acid having the nucleotide sequence of SEQ ID NO:1 and comprising at least one polymorphism as shown in Table 1;

(b) a nucleic acid molecule comprising an IRF6 nucleic acid having the nucleotide sequence of SEQ ID NO:1 and comprising at least two polymorphism as shown in Table 1; and

(c) a nucleic acid molecule comprising an IRF6 gene, the nucleotide sequence of SEQ ID NO:1 encoding a polypeptide comprising an amino acid sequence as depicted in SEQ ID NO:2 and comprises at least one polymorphism associated as shown in Table 1.

42. A vector comprising an isolated nucleic acid molecule comprising SEQ ID NO:1 and comprising at least one polymorphism shown in Table 1, operatively linked to a regulatory sequence.

43. A recombinant host cell comprising the vector of claim 42.

44. An isolated nucleic molecule comprising an IRF6 nucleic acid having a nucleotide sequence depicted in SEQ ID NO:1, wherein said nucleotide sequence encodes a polypeptide sequence comprising amino acids 13-113 of SEQ ID NO:2, wherein said polypeptide comprises at least one polymorphism as shown in Table 1.

45. An isolated nucleic molecule comprising an IRF6 nucleic acid having a nucleotide sequence depicted in SEQ ID NO:1, wherein said nucleotide sequence encodes a polypeptide sequence comprising amino acids 226-394 of SEQ ID NO:2, wherein said polypeptide comprises at least one polymorphism as shown in Table 1.

46. The isolated nucleic acid molecule of claim 44, said polymorphism is a change from arginine to a cysteine at amino acid residue 84 (Arg84Cys).

47. The isolated nucleic acid molecule of claim 46, said polymorphism is a change from a cytosine to a thymine at nucleotide position 250 (C250T).

48. The isolated nucleic acid molecule of claim 44 said polymorphism is a change from an arginine to a histidine at amino acid residue 84 (Arg84His).

49. The isolated nucleic acid molecule of claim 48, said polymorphism is a change from a guanine to an adenine at nucleotide position 251 (G251A).

50. An isolated nucleic acid molecule comprising: exons 2-9 of an IRF6 nucleic acid comprising SEQ ID NO:1, wherein at least one has at least one polymorphism as shown in Table 1.

51. An isolated polypeptide encoded by an IRF6 nucleic acid comprising:

(a) the amino acid sequence as depicted in SEQ ID NO:2 which comprises at least one polymorphism as shown in Table 1;

(b) the amino acid sequence as depicted in SEQ ID NO:2 which comprises at least two polymorphisms as shown in Table 1;

(c) an amino acid sequence which is greater than about 90% identical to an amino sequence of SEQ ID NO:2 which comprises at least one polymorphism as shown in Table 1; and

(d) an amino acid sequence which is greater than about 95% identical to an amino acid sequence of SEQ ID NO:2 which comprises at least one polymorphism as shown in Table 1.

52. A fusion protein comprising the polypeptide of claim 51.

53. An antibody, or an antibody fragment thereof, that specifically binds to the polypeptide of claim 51.

54. An antibody, or antibody fragment thereof that specifically binds to the polypeptide of claim 44.

55. An antibody or antibody fragment thereof that specifically binds to the polypeptide of claim 45.

56. An isolated nucleic acid comprising at least 20-50 contiguous nucleotides, wherein said nucleic acid comprises the nucleotide sequence of SEQ ID NO:1 and comprises at least one polymorphism as shown in Table 1.

57. The nucleic acid molecule of claim 41, wherein the nucleic acid is DNA.

58. The nucleic acid molecule of claim 41, wherein the nucleic acid is RNA.

59. The nucleic acid of claim 56, wherein the nucleic acid is DNA.

60. The nucleic acid of claim 56, wherein the nucleic acid is RNA.

61. An isolated polypeptide encoded by an IRF6 nucleic acid comprising: the amino acid sequence as depicted in SEQ ID NO:2, wherein said polypeptide sequence comprises a polymorphism of valine to isoleucine at amino acid residue 274 (V274Ile).

62. A pharmaceutical composition comprising the polymorphic nucleic acid of claim 41 and a physiologically acceptable carrier.

63. A pharmaceutical composition comprising the vector of claim 42, and a physiologically acceptable carrier.

64. A pharmaceutical composition comprising the polypeptide of claim 51, and a physiologically acceptable carrier.

65. A pharmaceutical composition comprising the fusion protein of claim 52, and a physiologically acceptable carrier.

66. A pharmaceutical composition comprising the antibody of claim 53 and a physiologically acceptable carrier.